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Review Article

Complications and Management of Rheumatic Mitral Valve Disease

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Abstract

Background: Mitral stenosis is a valvular heart disease characterized by the narrowing of the orifice of the mitral valve of the heart. It is almost always caused by rheumatic valvular heart disease. Mitral regurgitation (MR) is caused by the retrograde flow of blood from the left ventricle (LV) to the left atrium (LA) through the mitral valve (MV), which allows the systolic murmur to be heard best at the top of the heart with radiation to the left axilla.

Aim: This study overviews the pathophysiology, diagnosis, complications and management of rheumatic mitral valve diseases.

Conclusion: Rheumatic Mitral Valve Disease might happen in young age, it is mostly asymptomatic and only symptoms appear when they become. Management of the condition depends on the severity of the symptoms; surgical intervention could be used in severe cases while medications such as anticoagulants can work in mild conditions. Finally, more efforts should be paid to the low-income countries to help decrease the incidence of these diseases.

Keywords: *Mitral Valve Stenosis; Mitral Valve Regurgitation; Rheumatic Valve Disease*

Introduction

Acute rheumatic fever attacks that occur either as singular or multiple attacks can damage the valves of the heart, causing a chronic condition known as Rheumatic heart disease. That explains the high prevalence of rheumatic heart disease between 25 - 45 years old in adults, although the disease itself happens in childhood [1]. The most prevalent type of valvular heart disease in the United States is

degenerative valve disease, while in developed nations, rheumatic heart disease accounts for most valve pathology. ACR can occur due to infection from Group A *Streptococcus* (Strep A) bacterium, causing the body to develop an autoimmune response, without treatment the condition will worse causing repeated infections. Although the fever and other symptoms can resolve ARF-associated carditis lead to the damage of at least one valve of the heart, this on the long term can cause heart failure, stroke or premature mortality [2].

Rheumatic fever (RF) pathogenesis in susceptible people is linked to humoral and cellular autoimmune responses directed towards human tissues. This action is induced by hemolytic group A streptococci. Statistics show that 30 - 45% of rheumatic fever (RF) patients develop Rheumatic heart disease (RHD), different tissues of the heart are involved in the pathogenesis as it causes inflammation of pericardium, myocardium, and endocardium and eventually damage of heart valves [3]. The role of inflammation could is suggested due to presence of CD4 T cells and macrophages at the affected heart lesions [4,5]. CD4 and CD8 are found to be up-regulated and cause more invasions that is eased by presence of adhesion molecules such as VCAM-1 [6].

The prevalence of ARF and RHD is decreasing worldwide, but it is still high enough to be considered as endemic disease in some areas where healthcare is not available or in crowded places [7]. RHD lead to 500,000 deaths per year. Disease aged-standardized death rate pattern described by The Global Burden of Disease shows that in the time between 1990 - 2015 there was a decrease in the number of death due to RHD by 47.8% [8]. In developed countries, people who susceptible to the disease are those who are indigenous and migrant populations. In Australia for example 87% of the patients diagnosed with RHD came from Aboriginal and Torres Strait Islands [9].

In children between 5 - 14 years old, the occurrence of acute rheumatic fever and rheumatic heart disease is high. Its first episode however can occur in young kids aged 2 to 3 years of age [10-12]. Jones criteria is considered the main guideline in diagnosing the patients for acute rheumatic fever [13] many modifications have been applied to this criteria that led to high specificity but less sensitivity and finally this criteria became useless in conditions where the prevalence of the disease is high [14].

Although this improvement is very high, the problem is still in the developed countries as in non -endemic places the number of cases is very low and estimated to be 3.4/100,000, while in endemic regions this number increases to be 444/100,000. Oceania, South Asia and Central Sub-Saharan Africa are known to be the places with the highest death rates and prevalence [15]. It is clear that while the burden of RHD is enhanced in economically high countries, other low- income countries face terrible silent suffering and deaths each year.

Mitral stenosis is a valvular heart disease characterized by the narrowing of the orifice of the mitral valve of the heart. It is almost always caused by rheumatic valvular heart disease. Normally, mitral valve is about 5 cm^2 during diastole. Any decrease in area below 2 cm^2 causes mitral stenosis. Early diagnosis of mitral stenosis in pregnancy is very important as the heart cannot tolerate increased cardiac output demand as in the case of exercise and pregnancy.

Mitral regurgitation (MR) is caused by the retrograde flow of blood from the left ventricle (LV) to the left atrium (LA) through the mitral valve (MV), which allows the systolic murmur to be heard best at the top of the heart with radiation to the left axilla. MR is the most prevalent valve abnormality in the world, affecting more than 2% of the total population and having a frequency that rises with age. Mitral regurgitation arises from valve leaflet disorders or surrounding systems, which can allow the mitral apparatus to be compressed. Symptomatic heart failure is usually found in patients with acute severe MR due to lack of acceptance of rapid increase in volume load in their ventricles [16].

This study overviews the pathophysiology, diagnosis, complications and management of rheumatic mitral valve diseases.

Participants and Methods

Study design: Review article.

Study duration: Data were collected between 1 August and 30 November 2020.

Data collection: Medline and PubMed public database searches have been carried out for papers written all over the world on rheumatic mitral valve disease. The keyword search headings included "mitral valve stenosis, mitral valve regurgitation, rheumatic valve disease", and a combination of these will be used. For additional supporting data, the sources list of each research was searched. Criteria of inclusion: the papers have been chosen on the basis of the project importance, including one of the following topics: mitral valve stenosis, mitral valve regurgitation, rheumatic valve disease, etc.). Criteria for exclusion: all other publications that did not have their main purpose in any of these areas or multiple studies and reviews were excluded.

Statistical analysis

No predictive analytics technology has been used. In order to evaluate the initial results and the methods of conducting the surgical procedure, the group members reviewed the data. The validity and minimization of error were double revised for each member's results.

Pathophysiology

Chronic RHD is associated with pancarditis and has mitral valve involvement causing regurgitation in almost 100% of cases due to scarring of the valve and valve apparatus. Mitral regurgitation leads to left ventricular volume overload due to increased stroke volume, caused by an increase in blood volume within the left atrium and hence an increased preload delivered to the left ventricle during diastole [17]. In chronic progressive MR, ventricular remodeling occurs; allowing maintenance of cardiac output, and an initial increase in ejection fraction (EF) is usually observed [18].

Standard mitral orifice area is between 4 and 6 square centimeters. Under normal physiological conditions, the mitral valve is opened during the left ventricular diastole to allow blood to flow from the left atrium to the left ventricle. The pressure in the left atrium and the left atrium during the diastole is similar. The left ventricle is packed with blood in an early ventricular diastole [19].

Mitral valve areas smaller than 2 square centimeters block blood flow from the left atrium to the left ventricle which produces a gradient of strain around the mitral valve. If the gradient in the mitral valve rises, the left ventricle allows the atrial kick to be supplied with blood [20].

The mitral valve area of less than 1 square centimeter induces an increase in left atrial pressure. The standard diastolic pressure of the left ventricular is 5 mmHg. A pressure gradient of 20 mmHg through the mitral valve due to extreme mitral stenosis causes a left atrial pressure of around 25 mmHg. This left atrial pressure is passed to the pulmonary vasculature resulting in pulmonary hypertension [21].

Diagnosis

Physical examination

Mitral stenosis presents 20 to 40 years after an episode of rheumatic fever. The most common symptoms are orthopnea and paroxysmal nocturnal dyspnea. Patients may have symptoms of palpitations, chest pain, hemoptysis, thromboembolism when the left atrial volume is increased, ascites, edema, and hepatomegaly (if right-side heart failure develops).

However, patients with severe MR vary depending on the severity of decompensation. In patients with compensated MR, the carotid upstroke is sharp. However, in the case of advanced heart failure, the volume of the carotid pulse is decreased [22]. Clinical findings related to MR include significant dyspnea at rest, exacerbated in the supine position, as well as cough with clear or pink, frothy sputum. They may also endorse symptoms associated with myocardial ischemia, such as chest pain radiating to the neck, jaw, shoulders, or upper

extremities, nausea, and diaphoresis. Physical examination may reveal altered mental status, tachycardia (or bradycardia if there is ischemic involvement of the conduction system), hypotension, tachypnea, hypoxemia, and cyanosis [23].

Diagnostic testing

Chest radiography: Patients with chronic MR, cardiomegaly occur due to enlargement of LV and left atrium, also patients with HTN show right-sided chamber enlargement [16,21]. Mitral stenosis findings are normal heart size, straightening of the left border of the cardiac silhouette, prominent main pulmonary arteries, dilatation of the upper pulmonary veins and displacement of the esophagus by an enlarged left atrium. During the severe chronic stage of mitral stenosis, the chest x-ray will have enlargement of all the chambers, pulmonary arteries, and pulmonary veins.

Electrocardiography: Electrocardiography is the most important test in diagnosing MR patients. The most common ECG findings in patients with MR include left atrial enlargement and atrial fibrillation [21]. In mitral stenosis the P wave changes suggest left atrial enlargement. A presence of right axis deviation and right ventricular hypertrophy suggest severe pulmonary hypertension. ECG frequently detects atrial arrhythmias such as atrial fibrillation.

Complications

Before cardiac complications occur in late adulthood, rheumatic heart disease is usually dormant or silent. The most known complications are viral endocarditis, embolic attacks, heart failure, pulmonary hypertension, and atrial fibrillation from untreated extreme valve disease. The common complications of mitral stenosis are heart failure, strike, and endocarditis [24,25]. Pulmonary hypertension has been reported as a complication of mitral valve stenosis. Heart failure is also a known complication of mitral valve stenosis as mitral valve narrowing interferes with blood flow increasing pressure in lungs, leading to fluid accumulation that buildup strains in right side of the heart, leading to right heart failure. Heart enlargement due to pressure buildup of mitral valve stenosis has also been reported. Atrial fibrillation due to stretching and enlargement of heart's left atrium which lead to heart rhythm irregularity was reported. Blood clots caused by atrial fibrillation can travel to other body systems causing stroke if a clot blocks a blood vessel in brain [26].

Complications of mitral regurgitation include heart failure and related symptoms, atrial fibrillation, stroke due to arrhythmias, pulmonary artery hypertension and dilation of the heart and cardiomegaly [27].

A pre-study survey of common complications conducted by Okello, Emmy., *et al*. [8] concluded that among the total number of the patients in this study 90% had cardiovascular symptoms and about 50% had related complications which are higher than the percentage reported by Sani., *et al*. as it showed that 32% had left ventricular dysfunction [28]. When valve regurgitation or stenosis becomes severe, cardiovascular symptoms appear. This was seen in this study as 52% of patients had severe mitral regurgitation with a mean LVESD > 55 mm and symptoms were registered by 80% of these patients [29]. About 50% of the population was presented with a complication.

Pulmonary hypertension affected 1/3 of the total population; both Males and females were affected equally. It happened due to problems in mitral and aortic valve. Development of pulmonary hypertension decreases the quality of the patient's life and his life expectancy [30]. About 11% of the population showed Recurrent ARF, but they did not meet classical Jones criteria which show the importance of using 2003 WHO modification of the Jones criteria. The criteria met was, chorea, evidence of Group A streptococcal infection and Joint pains [31].

The third most common complication was atrial fibrillation as it was shown by about 14% of the patients. The most common continuous arrhythmia is atrial fibrillation and is correlated with complications such as heart failure, stroke and other embolic phenomena [32]. Okello, Emmy., *et al*. showed that atrial fibrillation had strong connection to heart failure as 81.4% of AF patients developed heart failure.

Also, as the formation of clots and stasis of the blood happens during atrial fibrillation, patients are most likely to develop cardio-embolic phenomena [8].

Okello, Emmy reported that only 4 patients had stroke [8] all of them had concurrent atrial fibrillation, all the patients was not using anticoagulant as physicians hesitate to prescribe anticoagulants in developing countries as it needs monitoring. Data shows decrease in the incidence of stroke when using anticoagulants. The treatment regimen should begin with low-molecular weight heparin and Coumadin at the time of anti-arrhythmia initiation [33].

Management

For years, patients with chronic MR may remain asymptomatic. However, in the absence of symptoms, serial clinical assessments and noninvasive testing are important because LV dysfunction can occur. Patients with a mild MR and normal heart can perform echocardiography with yearly clinical diagnosis only if their clinical state changed. After discussions on the value of early referral for surgery, asymptomatic patients who show severe symptoms of MR should be recommended for surgical repair, especially if the valve can be restored. If the patients reject surgery, they must be followed up every 6 - 12 months with clinical examination and echocardiography and should be immediately referred for surgery if signs, atrial fibrillation, pulmonary hypertension, or systolic LV dysfunction occur [34].

The key determinants of an appropriate outcome are surgical abilities and experience. Calcified mitral annulus, in comparison, or rheumatic activity of The MV reduces the chance of repair, even in experienced hands. Angiotensin converting enzyme inhibitors, β-blockers and biventricular pacing are proven to have beneficial reverse remodeling in patients with functional MR associated with LV dysfunction, and a decrease in LV end-diastolic and end-systolic volumes with these therapies is linked to reduce in MRR severity [35,36].

Surgical MV is the management of choice in patients with severe degenerative MR. If the operation is undertaken in a timely and effective manner by highly trained expertise in the field, the operative risk is low and life expectancy of patients is relatively higher. Restrictive annuloplasty should be done only in the early stages of the disease and in patients without echocardiographic predictors of postoperative residual or recurrent MR. Otherwise, MV replacement is preferable. Transcatheter correction of MR regurgitation, either through MV repair or MV replacement is a new emerging field of cardiovascular management and expected to have a substantial influence on surgical practice in the future [37].

In order to avoid recurrent rheumatic fever, patients with MS caused by rheumatic heart disease should obtain penicillin prophylaxis for β-hemolytic streptococcal infections. Anticoagulant therapy is recommended for the treatment of systemic embolism in any previous embolic events in patients with atrial fibrillation [38]. For percutaneous balloon valvotomy, symptomatic patients with serious MS or those with pulmonary hypertension should be considered. For this treatment, patients with severe MR, severely thickened or strongly calcified MV leaflets, are not optimal candidates. It is important to consider surgical valve replacement for patients who are not suitable for percutaneous intervention [39].

In patients with mitral stenosis, clinical and non-invasive results can be used to determine the need for therapeutic action. Mitral valve repair is indicated when mild dyspnea, resting dyspnea or pulmonary edema, hemoptysis, atrial fibrillation, chronic systemic embolism or right ventricular dysfunction occur in a patient with a mitral valve region of less than two centimeters, as shown by Doppler echocardiography [40].

Conclusion

Rheumatic Mitral Valve Disease might happen in young age, it is mostly asymptomatic and only symptoms appear when they become. Many tests could be conducted to determine the site where the heart is affected such as Chest Radiography and exercising tests. Manage-

ment of the condition depends on the severity of the symptoms; surgical intervention could be used in severe cases while medications such as anticoagulants can work in mild conditions. Finally, more efforts should be paid to the low-income countries to help decrease the incidence of these diseases.

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